

REMARKS

Claims 1-9, 11-30, and 37 are under consideration.

Claims 10 and 31-36 have been canceled without prejudice.

Claims 1, 11, 22, and 23 have been amended.

Claim 1 has been amended to specify that the claimed delivery vehicle comprises a plurality of separate, physiologically inert beads (i.e., each bead is a separate entity; the beads are not pellets or composites made up of small particles pressed together), that the beads have an average diameter in the range of 1 to 6 mm, and that each individual bead has the silver ion releasing composition coated on the surface of the bead. Support for this amendment can be found in original claim 10, in Figure 1, which shows an individual polymeric bead with a coating of silver nitrate composition on the surface of the bead, and in the specification at page 3, lines 9- 32, page 6, lines 19-22, page 7, lines 17-20, and page 9, lines 4-25.

Claim 11 has been amended to delete the term "substantially".

Claims 22 and 23 have been amended to replace the term "contain" with the term "bear" to be consistent with the language used in claim 1, which uses the term "bearing" rather than "containing".

No new matter is added by these amendments.

Rejections under 35 U.S.C. §112.

Claim 11 was rejected as allegedly being indefinite for using the term "substantially" spherical. The term "substantially" as used in the claim, was merely meant to convey what is in fact the case, i.e., that no bead, no composition of matter, can be perfectly spherical, since all matter is inherently non-uniform to some extent. While applicants do not agree that the term "substantially" is indefinite in this case, nonetheless, the term has been deleted from the claim in the interests of facilitating prosecution. Applicants do not deem or intend this amendment to limit or change the scope of the claim in any way.

Rejections under 35 U.S.C. §102.

Claims 1, 2, 8, 9, 12, 16-18, 24, 25, 28, 30, and 37 stand rejected under 35 U.S.C. §102 (b) as allegedly being anticipated by Kodama *et al.*; claims 1-3, 6, 8, 10-13, 24-26, 28, 30, and 37 stand rejected under 35 U.S.C. §102 (b) as allegedly being anticipated by Tsukisaka *et al.*; claims 1-3, 6, 8, 9, 12, 13, 24, 25, 28-30, and 37 stand rejected under 35 U.S.C. §102 (b) as allegedly being anticipated by Hirai *et al.*; and claims 1-3, 6, 8, 12, 13, 24-27, and 37 stand rejected under 35 U.S.C. §102 (b) as allegedly being anticipated by Siiman *et al.*

The rejections based on Kodama *et al.*, Hirai *et al.*, and Siiman *et al.* are no longer applicable, since claim 1 has been amended to include the size limitation of cancelled claim 10, which was not included in the anticipation rejections based on these references, since these references do not teach or suggest this limitation.

Claims 1-3, 6, 8, 10-13, 24-26, 28, 30, and 37 are patentable over Tsukisaka *et al.*, as well. The presently claimed silver ion delivery vehicle comprises a plurality of separate, physiologically inert beads bearing a tissue necrosing amount of a water soluble silver ion releasing compound coated on the surface of each bead, the beads having an average diameter in the range of about 1 to about 6 millimeters. In contrast, Tsukisaka *et al.* is directed to an antibiotic bead prepared by solidifying a powdery substance in bead form with a binder consisting of an antibiotic metal salt of an organic polymer (see the translated abstract). Thus, the beads of Tsukisaka *et al.* are composites in which the metal salt is intimately mixed with the binder and a powdered support material to form the bead. Bead sizes specified in this reference refer to the composite bead, after being bound together. This is distinguishable from the present invention, in which the beads are discrete, individual beads (not composites) having an average diameter in the range 1 to 6 mm.

Because the majority of silver is coated on the surface of the beads, the beads of the present invention rapidly release a tissue necrosing amount of silver ion upon contact with the uterine lining for treatment of menorrhagia (i.e., by chemical cauterization of the uterine lining). The beads of Tsukisaka *et al.* would not be suitable for the intended purpose of the present invention. For example, according to paragraph [0025] of the machine translation of Tsukisaka *et al.*, the obtained beads demonstrate antibacterial action over a long

time. This indicates that the release of silver ions is slow and would be inefficient or ineffective for cauterizing the uterine lining, which requires rapid, localized delivery of silver ions. In addition, if the binder of Tsukisaka *et al.* were selected to be water soluble or partially water soluble to speed up dissolution of the silver ions, such composite beads could partially or completely break up into a powder upon dissolution of the metal salt and/or binder. This would be undesirable for use in the uterus, because it would be very difficult, if not impossible, to determine whether all of the beads placed into the uterus has been completely removed after the cauterization procedure. The beads of the presently claimed invention, on the other hand, are solid, non-composite materials, and will not disintegrate during treatment. Thus, the beads can be counted before and after the cauterization procedure, insuring that all of the beads have been removed from the uterus. Accordingly, the present rejection is unwarranted and should be withdrawn, since the composite materials of Tsukisaka *et al.* are not suitable for treatment of menorrhagia and the reference does not teach or suggest the presently claimed invention.

Rejections under 35 U.S.C. §103(a).

Claims 1-7 stand rejected under 35 U.S.C. §103 (a) as allegedly being obvious over Tsukisaka *et al.* As noted above, this reference teaches a composite bead, not the presently claimed beads. There is no teaching or suggestion in this reference that would have led one of ordinary skill in the art to prepare the claimed delivery vehicle at the time the invention was made. Furthermore, the teachings of this reference provide for a product (composite beads) that is not suitable for the intended purpose of the present delivery vehicle. Thus, Applicants request that the present rejection be withdrawn.

Claims 1, 10, 11, and 19-23 also stand rejected under 35 U.S.C. §103 (a) as allegedly being obvious over Hirai *et al.* in view of Block. This rejection is unwarranted, as well.

Hirai *et al.* disclose a particle bearing composite material, which comprises a solid carrier and polymer-protected particles adsorbed onto the surface of the solid support. The particles are a polymer-stabilized colloidal suspension of metallic or metal compound particles. Metallic particles disclosed in this reference are particles of palladium, rhodium,

ruthenium, platinum, iridium, osmium, silver, gold, and copper. The colloidal dispersion of metal particles can be made by reduction of a metal salt, such as silver nitrate (i.e., silver nitrate is disclosed only as a precursor for production of metallic silver; see col. 3, line 58 through col. 4, line 19). Metal compounds disclosed in this reference are metal borides, metal sulfides, metal hydroxides, and metal oxides (see col. 4, lines 20-61).

Metal borides and sulfides, such as silver sulfide, are well known to be highly insoluble, as are many metal oxides (See, e.g., Cotton & Wilkinson *ADVANCED INORGANIC CHEMISTRY*, Fifth Ed., Wiley Interscience (1988), pages 165 and 939-954, hereinafter "Cotton & Wilkinson", a copy of which is attached hereto). Under basic conditions, silver ion spontaneously forms silver oxide (see Cotton & Wilkinson, page 942, where the log of the equilibrium constant (log K) is -7.42 for the formation of silver ion from silver oxide and -5.75 for the formation of silver hydroxide from silver oxide, indicating that the spontaneous reaction is in the direction of silver oxide formation, not silver ion or silver hydroxide formation). Thus, the teachings of Hirai *et al.* are inapposite to the present claims, since silver metal, silver boride, silver sulfide, and silver oxide are quite insoluble and would not readily release silver ions in amounts sufficient to cause tissue necrosis, as required by the claims. Furthermore, the teachings of Hirai *et al.* are directed to catalyst materials, not to compositions for medical treatment such as silver ion delivery vehicles for treating menorrhagia, as presently claimed.

The Office Action states that Block describes the use of a mixture of silver nitrate and silver chloride for cauterizing wounds and removing warts. The caustic nature of silver nitrate is not in dispute, however. The issue is whether a person of ordinary skill in the art would have been motivated to combine the teachings of Hirai *et al.* with Block. He or she would not. These references are directed to entirely different fields (catalysts versus disinfectants), and one of ordinary skill in the art would not have been motivated to replace the metallic or insoluble metal compounds taught by Hirai *et al.* with the *soluble* silver salts taught by Block to arrive at the silver ion delivery vehicles of the present invention. There is no indication in Hirai *et al.* that silver nitrate can act as a catalyst. In fact, the only use of silver nitrate disclosed in Hirai *et al.* is for preparing colloidal silver metal.

Furthermore, there is no teaching or suggestion in Block that would have led

one of ordinary skill in the art to look to Hirai *et al.* for guidance in preparing a silver ion delivery vehicle for treating menorrhagia. Hirai *et al.* teaches the use of a colloidal suspension of polymer coated metallic particles or metal compound particles adsorbed on a solid support. There is no teaching or suggestion in either Hirai *et al.* or Block as to whether or how silver nitrate or any other soluble silver salt can be made into a colloidal suspension. In addition, Hirai *et al.* distinguishes soluble metal salts (e.g., silver nitrate) from the metal "compounds" which are clearly meant to be insoluble materials. One of ordinary skill in the art would not have had a reasonable expectation that such insoluble particles could be replaced by soluble salts. The references simply do not teach or suggest that a soluble silver salt can be used in place of the metallic or metal compound particles of Hirai *et al.*.

Accordingly, the present claims are patentable over the combined teachings of Hirai *et al.* and Block, since these references are not properly combinable, and one of ordinary skill in the art would not have had a reasonable expectation of success in obtaining the presently claimed silver ion delivery vehicle for treating menorrhagia based on the teachings of these references, even if they were combined.

Claims 1, 12, 14, and 15 stand rejected also stand rejected under 35 U.S.C. §103 (a) as allegedly being obvious over Kodama *et al.* Amended claim 1 includes the size limitation of cancelled claim 10, which was not included in the rejection, since Kodama *et al.* does not teach or suggest this limitation. Accordingly, this rejection should be withdrawn, as well.

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Conclusion.

The present claims are patentable over the applied references.

Reconsideration, allowance of all pending claims, and early passage of the application to issue is earnestly solicited.

Respectfully submitted,

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